

Original Research Article

A study to assess the correlation between HbA1c and microalbuminuria among diabetics

Sruthi Kare, Vishwantha N. Reddy*, Thejdeep Mahamkali

Department of General Medicine, Sri Devraj Urs Academy of Higher Education and Research, Kolar, Karnataka, India

Received: 14 November 2020

Revised: 04 December 2020

Accepted: 05 December 2020

*Correspondence:

Dr. Vishwanath N. Reddy,

E-mail: statisticsclinic2018@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: India is one of the epicentres of the global diabetes mellitus pandemic. Rapid socioeconomic development and demographic changes, along with increased susceptibility for Indian individuals, have led to the explosive increase in the prevalence of diabetes mellitus in India over the past four decades. Diabetic Nephropathy is a common consequence of long-standing diabetes mellitus. The development of diabetic nephropathy has a dramatic increase on the morbidity and mortality of patients with diabetes. Objective of this study was to evaluate the prevalence of microalbuminuria in patients with diabetes mellitus patients.

Methods: This cross-sectional study was conducted on T 2 diabetes mellitus patients visiting medicine OPD of R L Jalappa hospital constituent hospital of Sri Deveraj Urs Medical College, Tamaka, Kolar from May 2016 to July 2016. A total of 60 type-2 diabetes patients were enrolled in the study.

Results: Average duration of diabetes among study group was 8 years and most of the patients were between 6-10 years. In type 2DM patients, microalbuminuria and glycemic control have shown a significant linear correlation with duration of diabetes ($p < 0.05$). Also, micro albuminuria has a significant correlation with increase in level of glycosylated haemoglobin.

Conclusions: The prevalence of microalbuminuria in diabetic patients was found to be high and being a developing country; there is a dire need that microalbuminuria and HbA1c testing should be done in both, newly diagnosed as well as already diagnosed type 2DM patients as an early marker of renal risk factor.

Keywords: Microalbuminuria, Glycemic control, Diabetic, Nephropathy, Elderly

INTRODUCTION

Diabetes is an important metabolic disorder worldwide and is characterized by variable degree of insulin resistance, impaired insulin secretion, and increased glucose production.¹

India is one of the epicentres of the global diabetes mellitus pandemic. Rapid socioeconomic development and demographic changes, along with increased susceptibility for Indian individuals, have led to the explosive increase

in the prevalence of diabetes mellitus in India over the past four decades.²

The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs. Noninsulin dependent diabetes mellitus (NIDDM) type 2 occurs at any age, but is more common between 40-80 years of age and also has a strong genetic component.³ Patients with type 2 diabetes often have a long asymptomatic period of hyperglycaemia and many have complications at the time of diagnosis. Microvascular

complications including nephropathy, retinopathy and neuropathy are initiated by chronic hyperglycemia. Many association studies suggested a strong correlation between level of hyperglycemia and the progression of microvascular complications in diabetic patients.⁴

Major risk factors for type 2 diabetes mellitus are age \geq 45 years, overweight-BMI \geq 25 kg/m², family history of diabetes mellitus, habitual physical inactivity, race/ethnicity (e.g. African-Americans, hispanic Americans, native Americans, Asian Americans), previously identified IFG or IGT, history of gestational diabetes mellitus or delivery of baby weighing \geq 9 lbs, hypertension \geq 140/90 mmHg, HDL cholesterol \leq 35 mg/dl and or triglyceride \geq 250 mg/dl, central obesity (WHR men \geq 1, women \geq 0.85).⁵

Diabetic nephropathy is a common consequence of long-standing diabetes mellitus. The development of diabetic nephropathy has a dramatic increase on the morbidity and mortality of patients with diabetes.⁶ Diabetic nephropathy rarely develops before ten years duration of diabetes. The annual incidence of diabetic nephropathy in IDDM peaks just before 20 years and thereafter declines. Studies in type-2 diabetes show similar results to those in IDDM. It is characterized by the presence of large amounts of urinary proteins, mostly albumin. Diabetic-nephropathy is the leading cause of end stage renal disease (ESRD) in US and a leading cause of diabetes mellitus related morbidity and mortality.⁷

Mogenson has classified diabetic nephropathy into 5 stages, stage 1 (0-2 years)- stage of hyper filtration and hyper perfusion, is characterized by increased GFR, increase in renal size and reversible albuminuria unmasked by stress or exercise, Stage 2 (2-5 yrs)- stage of structural changes - characterized by increase in glomerular basement membrane thickness and increase in mesangial matrix, stage 3 (5-10 years)- stage of microalbuminuria or incipient diabetic nephropathy - defined as a urinary albumin excretion rate of 20-200 μ g/min or 30-300 mg/24 hrs. Microalbuminuria is predictive of development of overt proteinuria, stage 4 (10-15 years)- stage of overt proteinuria and renal failure- once proteinuria is established, renal function declines in exorably, stage 5 (15-25 years)- end stage renal disease - when GFR declines to less than 10 ml/min, the need for renal replacement in form of dialysis or renal transplantation is required.⁸

Microalbuminuria is an earliest marker of nephropathy and cardiovascular disease (CVD) in patients with diabetes and defined as a urinary albumin excretion rate (AER) between 30-300 mg/24 hrs or 20-200 μ g/min in a timed specimen or 30-300 mg/g of creatinine in a random specimen. Microalbuminuria develops in 30-40% of both type-1 and type-2 diabetes after duration of 20 years. Although microalbuminuria is predictive of worsening microvascular disease in the kidney (5-10% per year progress to overt diabetic nephropathy), an increased albumin excretion rate (AER) reflects a generalized

abnormality of vascular function and is associated with 2-4-fold increases in cardiovascular and all-cause mortality.⁹

The importance of microalbuminuria was first appreciated in the early 1980s when two landmark studies in London and Denmark independently reported that it was predictive of development of overt diabetic nephropathy and progressive renal failure.¹⁰

Pathogenesis appears to involve complex interactions between genetic and environmental factors. The pathophysiological basis for elevated urinary albumin excretion entails the binding of glucose to proteins resulting in excessive protein glycosylation with the build-up of advanced glycated end products. This leads to deposition of advanced glycated end products on the glomerulus resulting in renal and glomerular hypertrophy, mesangial matrix accumulation and thickening of glomerular basement membrane.¹¹ This abnormality permits the leakage of low molecular weight proteins [albumin]. This is the stage of microalbuminuria (incipient nephropathy) which could be reversible with good glycemic control. However, with persistent microalbuminuria, further leakage of protein in urine will result in overt diabetic nephropathy.¹² Increased level of microalbuminuria is associated with increased risk of progressive kidney disease leading towards end stage renal disease.

HbA1c is a blood glucose control marker in diabetic patients. Glycosylated hemoglobin (HbA1c) results from post-translation changes in the hemoglobin molecule, and their levels correlate well with glycemic levels over the previous six to ten weeks. Glycosylation of hemoglobin takes place under physiological condition by a reaction between glucose and N-terminal valine of beta chain of molecules. Higher levels of HbA1C were associated with increased risk for development of microangiopathy in diabetic. This may be due to the fact that HbA1c has special affinity for oxygen thereby causing tissue anoxia and plays a role in causation of micro and macroangiopathy.¹³

Thus, the present study was carried out to evaluate microalbuminuria in relation to HbA1c and duration of diabetes. Microalbuminuria and glycosylated haemoglobin were measured as risk markers of renal damage and glycemic control respectively.

Aims and objectives

Aim and objective were to evaluate the prevalence of microalbuminuria in patients with diabetes mellitus patients and to find the correlation between microalbuminuria and HbA1C.

METHODS

This cross-sectional study was conducted on T 2 diabetes mellitus patients visiting medicine OPD of R L Jalappa hospital constituent hospital of Sri Deveraj Urs Medical

College, Tamaka, Kolar from May 2016 to July 2016. Ethical approval was granted by the ethical review committee of SDUMC, Kolar. A total of 60 type-2 diabetes patients were enrolled in the study. A structured questionnaire regarding the demographic data such as age, sex, duration of diabetes. Blood pressure, smoking habit, family history of diabetes, renal disease and hypertension was recorded for each patient. Patients with systemic diseases like cardiovascular diseases, cerebrovascular diseases and urinary tract infection were excluded from the study. Consent from subjects and controls were taken before commencing the study.

A sample of blood was drawn after overnight fasting of 10-12 hours to test for HbA1c levels. The fasting blood sample with EDTA was used to estimate HbA1c levels. The samples were centrifuged, separated and stored at 4°C until analysis. The blood samples were analyzed for HbA1c (immuno-inhibition method), fasting blood glucose and postprandial blood glucose (GOD-POD), serum urea (urease method), and serum creatinine (Jaffe’s Kinetic). Urine sample was analyzed for microalbumin (immunoturbidimetric method). The multigent microalbumin immunoturbidimetric that uses polyclonal antibodies against human albumin was used for the determination of urine microalbumin urea.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Catagorical data was represented in the form of Frequencies and propotions. Pearson correlation coefficient was calculated to find the linear relation between HbA1C and microalbuminuria. T test was also used to find out relationship between HbA1c and microalbuminuria. P value was taken as significant at 5 percent confidence level (p<0.05).

RESULTS

A total of 60 study subjects were analysed in the present study. Among the 60 type 2DM patients studied most of patients were in the age group of 51-60 years (30%) and 61.66% were males and 38.33% were females with 43.33% patients having a family history of diabetes (Figure 1).

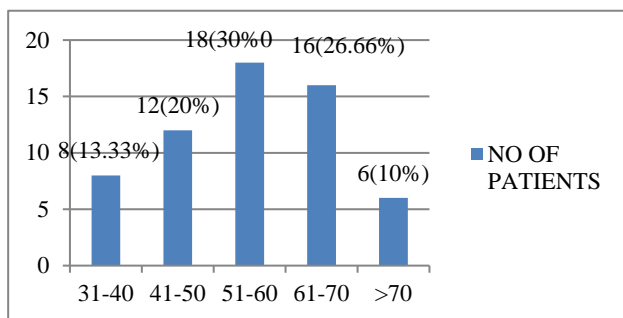


Figure 1: Age wise distribution of patients.

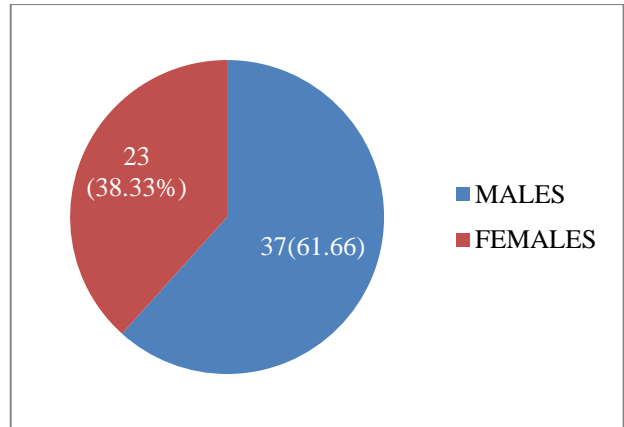


Figure 2: Distribution of females and males with diabetes mellitus.

Table 1: Duration of diabetes.

Duration of diabetes (years)	No of patients	Percentage
1-5	24	40
6-10	23	38.33
11-15	7	11.66
16-20	6	10

The average duration of diabetes among study group was 8 years and most (40%) of the patients were between 1-5 years. 38.33% of them were between the duration of 6-10 years of diabetes, 11.6% had history of diabetes for 11 to 15 years of duration and 10% more than 15 years history of diabetes (Table 1) and (Figure 2).

Table 2: No of patients with family h/o diabetes.

Family h/o diabetes	No of patients	Percent
Present	26	43.33
Absent	34	56.66

Nearly 56.66% of the study subjects had no family history of diabetes mellitus (Table 3). The mean fasting blood sugar level was found to be 172.15 mg/dl, PPBS was 238.63 mg/dl and HbA1C was 9.12%.

Table 3: Various lab parameters in study group.

Lab parameters	Average
FBS (mg/dl)	172.15±63.52
PPBS (mg/dl)	238.63±94.05
HbA1C%	9.12±5.6

In type 2DM patients, microalbuminuria and glycemic control have shown a significant linear correlation with duration of diabetes (p<0.05). Also micro albuminuria has a significant negative correlation with increase in level of glycosylated haemoglobin (Table 4).

Table 4: Correlation between HbA1c and microalbuminuria.

		hba1c	Microalbumin uria (mg/l)
hba1c	Pearson correlation	1	-0.077
	Sig. (2-tailed)		0.559
	N	60	60
Microalbumin uria (mg/l)	Pearson correlation	-0.077	1
	Sig. (2-tailed)	0.559	
	N	60	60

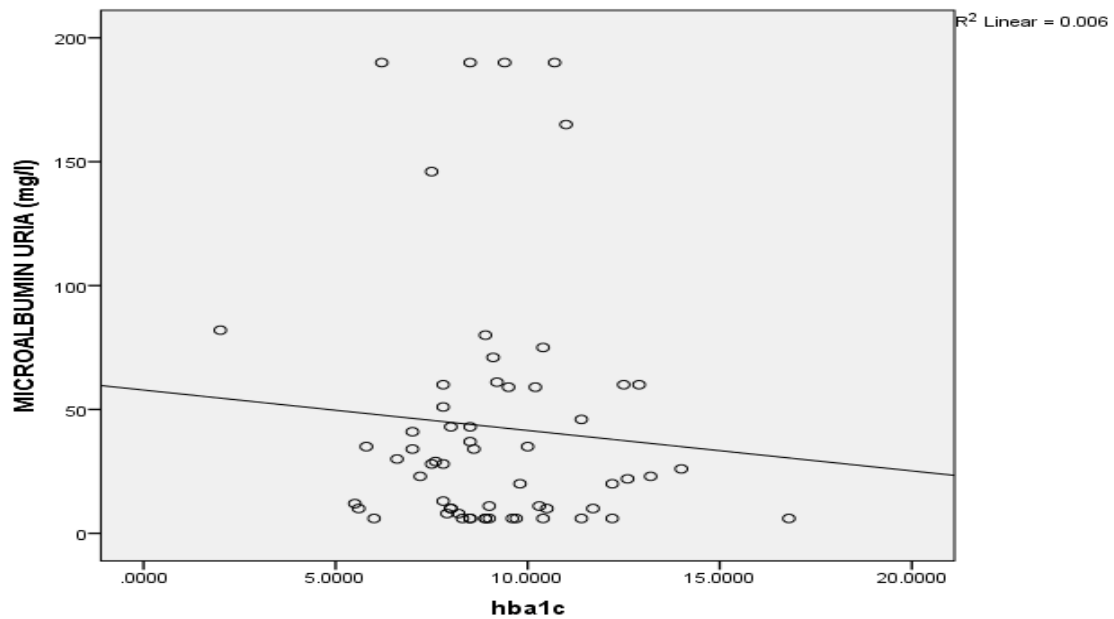


Figure 3: Scatter plot of HbA1c and microalbuminuria among study subjects.

DISCUSSION

Diabetes mellitus has become a major health problem in India. It has been estimated that the burden of type 2 DM for India is projected to increase to 87 million in 2030. The impacts of type 2 DM are considerable: as a lifelong disease, it increases morbidity and mortality and decreases the quality of life. At the same time, the disease and its complications cause a heavy economic burden for diabetic patients themselves, their families and society.

In our study, 40% patients had family history of diabetes showing that type 2 DM has a strong genetic component. Usually the patients are asymptomatic until complications become obvious and among those affected one-third will eventually have progressive deterioration of renal function.

The present study was conducted on 60 diabetic patients. The serum glucose is a continuous variable, rising and falling about two-fold throughout the day in people without diabetes, and up to some 10-folds in people with diabetes. Hence, the higher mean value of glycated hemoglobin in uncontrolled diabetes was expected in view of increase in microalbuminuria levels. This is based on the previous fact that HbA1c can provide an accurate and

reliable method to routinely assess the relative level of diabetes control.

In the present study micro-albuminuria has a highly significant correlation with HbA1c ($p < 0.05$), similar to the study reported by Kassab et al.¹⁴ The complications of both type 1 and 2 diabetes do not develop or progress for 6-9 years when the average HbA1c level is kept at $< 7\%$.¹⁹ The present study found an increase in HbA1c levels as indicated by a mean value of 9.¹² This shows that the population under study had poor glycaemic control.

The frequency of microalbuminuria increased with the increase in duration of diabetes. Microalbuminuria had a highly significant correlation with duration of diabetes $p < 0.001$. Population in the present study had an early onset of microalbuminuria, similar to that reported in an earlier study.

Zelmanovitz et al studied a total of 167 diabetic patients (20 type-1 and 147 type-2 diabetic patients; 78 women and 89 men), aged 20-84 years (Normoalbuminuric (n=84), microalbuminuric (n = 78) and macroalbuminuric (n=55) patients). And urinary protein concentration and urinary protein-to-creatinine ratio were measured. They concluded that measurements of proteinuria presented almost perfect

accuracy for the screening and diagnosis of overt diabetic nephropathy. Protein measurement in spot urine is a reliable and simple method for the screening and diagnosis of overt diabetic nephropathy.¹⁵

Joshi PP et al studied 158 cases of first AMI admitted at ICCU, Government Medical College and Hospital, Nagpur, India. Microalbuminuria was present in 66 (42%) cases as compared with 15 (20%) controls. Patients with microalbuminuria also had significantly higher frequency of heart failure (16 out of 66 patients (24%) Vs 11 out of 92 (12%), and had higher mortality (8 out of 66 (12%) Vs 3 out of 92 (3%), as compared to those without microalbuminuria and concluded that microalbuminuria is an independent risk factor for AMI and is associated with higher in-hospital heart failure and mortality in AMI. Microalbuminuria helps in risk stratification.¹⁶

In a study by Shehnaz A and Baig JA et al a study done from July to December 2007 on 100 known diabetic patients concluded that early onset of microalbuminuria in selected community could be due to poor glycemic control (high HbA1c >7% or hereditary factors). Screening microalbuminuria and HbA1c test should be done in both newly and already diagnosed type 2 diabetes patients as an early detection of renal dysfunction.¹⁷

Naveen et al evaluation on HbA1c and microalbuminuria as early risk marker for nephropathy in type 2 diabetes a study done in Malemarvathur, Tamilnadu, INDIA a cross sectional study done on uncontrolled type 2 diabetes and controlled and healthy controls were mean HbA1c, microalbuminuria and serum creatinine was highest in uncontrolled diabetes i.e. (8.01+0.83), (12+49.89), (2.18+1.12) when compared to control diabetes (6.49+0.37), (47.31+39.15) and (0.85+0.32) respectively so it concluded that risk of microalbuminuria increase with poor glycemic control.¹⁸

Chang et al a study on HbA1c variability is associated microalbuminuria in type 2 diabetes: a 7 years prospective cohort study published in 26th august 2012 when study was done between 2002 and 2005 where 821 middle aged normoalbuminuric individuals with type 2 diabetes who were followed up till 2010 incidence of microalbuminuria was 91.9/1000 persons for Q1-Q4 adjusted HbA1c SD respectively. So, it concluded that HbA1c variability even measured as early as 2 years is independently associated with development micro albuminuria in patients with type 2 diabetes.¹⁹

Khundu et al study in Kar RG medical college Kolkata, West Bengal India study on 50 males and 50 females type 2 diabetes of age group 30-60 years without any complications were taken as cases and 50 healthy cases of comparable age and sex were taken as controls and said that urine micro albuminuria, HbA1c levels were higher in cases.²⁰

In the study done by Varghese et al there was statistically correlation was found between the prevalence of microalbuminuria and the age of patients similar to our study.²¹ Similar results were also found from Naz et al reported the finding from the patients from Rawalpindi/Islamabad.²²

CONCLUSION

The prevalence of microalbuminuria in diabetic patients was found to be high and Being a developing country; there is a dire need that microalbuminuria and HbA1c testing should be done in both, newly diagnosed as well as already diagnosed type 2-DM patients as an early marker of renal risk factor. Hence, patients and health care givers should give very high priority to improving glycemic control sufficiently to maintain blood glucose. If this is achieved, the number of patients with microalbuminuria will decline substantially and in turn lower the numbers in which overt macroalbuminuria and end stage renal disease develop.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabet Care. 2003;26(1):5-20.
2. Satchell S, Tooke JF. What is the mechanism of microalbuminuria in diabetes: a role for the glomerular endothelium? Diabetologia. 2008;51:714-25.
3. Powers AC. Diabetes Mellitus. In: Jameson JL. (editor) Harrison's Endocrinology. 1st ed. New York: McGraw-Hill. 2006:303-4.
4. Mason RM, Wahab NA. Extracellular matrix metabolism in diabetic nephropathy. J Am Soc Nephrol. 2003;14:1358-73.
5. Vergouwe Y, Soedamah-Muthu SS, Zgibor J, Chaturvedi N, Forsblom C, Snell-Bergeon JK, et al. Progression to microalbuminuria in type 1 diabetes: development and validation of a prediction rule. Diabetologia. 2010;53:254-62.
6. American Diabetes Association. Testing in Asymptomatic Patients. Diabet Care. 2011;34(1):13-4.
7. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabet Care. 2011;34(1):62-9.
8. Bajaj S, Kannan V. Renal diseases in diabetes mellitus: Type-2 Diabet Melli. 2004:172-94.
9. Gupta SK, Singh Z, Purty AJ, Kar M, Vedapriya D, Mahajan P et al. Diabetes prevalence and its risk factors in rural area of Tamil Nadu. Ind J Comm Med. 2010; 35:396-9.

10. Viberti G, Mackintosh D, Rudolf W, Bilous, John C. Pickup, And Harry Keen. 'Proteinuria In Diabetes Mellitus: Role Of Spontaneous And Experimental variation of glycemia". *Kidney Int.* 1982;21(5):714-20.
11. Parving HH, Oxenball B, Svendsen PA, Christiansen J S and Andersen AR. Early edetection of patients at risk of developing diabetic nephropathy: a longitudinal study of urinary albumin excretion". *Acta endocrin (Copenh).* 1982;100:550-5.
12. Viberti GC, Hill Rd, Jarrett RJ, Argyropoulos A, Mahmud U, Keen H. Microalbuminuria as a predictor of clinical nephropathy in insulin dependent diabetes mellitus. *Lancet.* 1982;1:1430-2.
13. Mogensen CE, Christensen CK. Predicting diabetic nephropathy in insulindependent patients. *N Engl J Med.* 1984;311:89-93.
14. Kassab A, Ajmi T, Issaoui M, Chaeib L, Miled A, Hammami M. Homocysteine enhances LDL fatty acid peroxidation, promoting microalbuminuria in Type 2 diabetes. *Ann Clin Biochem.* 2008;45:476-80.
15. Zelmanovitz T, Gerchman F, Amely P, Balthazar S, Fúlvio CS, Thomazell, Jorge D Matos and Luís H Canani. Diabetic nephropathy. *Diabetol Metabol Synd.* 2009;1(4):1-17.
16. Joshi PP, Nirwan D, Holay MP, Salkar RG. Significance of Microalbuminuria in Acute Myocardial Infraction. *J Assoc Physic Ind.* 2003;51:1-10.
17. Sheikh SA, Baig JA, Iqbal T, Kazmi T, Baig M, Syed Husain S. Prevalence of microalbuminuria with relation to glycemic control in type-2 diabetic patients in Karachi. *J Ayub Med Coll Abbottabad.* 2009;21(3):83-6.
18. Naveen P. Evaluation of Glycated hemoglobin and Microalbuminuria as early risk markers of Nephropathy in Type 2 Diabetes Mellitus. *Int J Biol Med Res.* 2012;3(2):1724-6.
19. Hsu CC, Chang HY, Huang MC, Hwang SJ, Yang YC, Lee YS, et al. HbA1c variability is associated with microalbuminuria development in type 2 diabetes: a 7-year prospective cohort study. *Diabetologia.* 2012;55(12):3163-72.
20. Kundu D, Roy A, Mandal T, Bandyopadhyay U, Ghosh E, Ray D. Relation of microalbuminuria to glycosylated hemoglobin and duration of type 2 diabetes. *Nige J Clinic Pract.* 2013;16(2):216-20.
21. Varghese A, Deepa R, Rema M, Mohan V. The prevalance of microalbuminuria in Type 2 diabetes mellitus at a diabetes center in southern India. *Postgrad Med J.* 2001;77:399-402
22. Naz S, Sadaruddin A, Khannum A, Osmani R. Frequency of microalbuminuria in diabetic patients of Islamabad and Rawalpindi. *Pak J Med Res.* 2007;46(3):70-4.

Cite this article as: Kare S, Reddy VN, Mahamkali T. A Study to assess the correlation between HbA1c and microalbuminuria among diabetics. *Int J Adv Med* 2021;8:16-21.